

IN THE CLAIMS:

Claim 1 (original) A peptide derivative peptidomimic having general formula  $X-CX_1-NH-AA_1-CONH-AA_2$  wherein X is a heterocyclic or unusual amino acid,  $X_1$  is O or  $H_2$  and  $AA_1$  and  $AA_2$  are amino acids.

Claim 2 (original) A peptide derivative according to claim 1 wherein X is a heterocyclic selected from the group consisting of F-moc-3- (2-furyl)-L-alanine, F-3- (3-thienyl)-L-alanine, 4-Fmoc-piperazine-1-yl-acetic acid hydrate, Fmoc-3, 3-diphenyl-L-alanine, 1-Fmoc-azetidine-3-carboxylic acid, Benzimidazolepropionic acid, Fmoc1, 2,3,4 tetrahydroquinoline-3-carboxylic acid, 2-oxo-4-phenyl-3-oxazolidine-acetic acid, 5-Methoxy-2-methyl-3-indole acetic acid and 5-Mercapto-1-terazole acetic acid.

Claim 3 (original) A peptide derivative according to claim 1 wherein X is an unusual amino acids selected from a group consisting of 5-Hydroxytryptophan, L-Abrine, L- $\beta$ -homoproline,  $\beta$ -HomoTrp -OH, Homophenylalanine L- $\beta$ -homotryptophan, L-2-propargyl glycine, 3,3 Diphenylalanine, L- $\beta$ -Homohydroxyproline and Cyclohexylalanine.

Claim 4 (original) A peptide derivative according to claim 1 wherein the dipeptide for position  $AA_1-AA_2$ , is selected from the group consisting of Orn-Pro, Cha-Pro, Ile-Pro, Dap-Pro, Val-Trp, Lys-Pro, Lys-Trp, Orn-Trp, Dap-Trp, Ile-Phe,  $\beta$ -Ala-Pro, Pro-Pro and Cha-Trp.

Claim 5 (original) A peptide derivative according to claim 1 wherein the derivative represented by general formula  $X-CX_1-NH-AA_1-CONH-AA_2$  is selected from the group consisting of:

(a) L-Abrine- Orn-Pro, 3- (3-thienyl)-L-alanine- Orn-Pro, 3- (2-furyl)-L-alanine- Orn-Pro, 2-Benzimidazoleacetic acid- Orn-Pro, 5-Hydroxytryptophan- Orn-Pro, Homotryptophan- Orn-Pro, Homophenylalanine- Orn-Pro, 1,2,3,4-tetrahydro isoquinoline-3-carboxylic acid- Orn-Pro, Azetidine-3-carboxylic acid- Orn-Pro, Cyclohexylalanine- Orn-Pro, 2-Oxo-4-phenyl-3-oxazolidine acetic acid- Orn-Pro, 4 – piperazine acetic acid- Orn-Pro

(b) L-Abrine- Cha-Pro, 3- (3-thienyl)-L-alanine- Cha-Pro, 3- (2-furyl)-L-alanine- Cha-Pro, 2-Benzimidazoleacetic acid- Cha-Pro, 5-Hydroxytryptophan- Cha-Pro, Homotryptophan- Cha-Pro, Homophenylalanine- Cha-Pro, 1,2,3,4-tetrahydro isoquinoline-3-carboxylic acid- Cha-Pro, Azetidine-3-carboxylic acid- Cha-Pro, Cyclohexylalanine- Cha-Pro, 2-Oxo-4-phenyl-3-oxazolidine acetic acid- Cha-Pro, 4 – piperazine acetic acid- Cha-Pro

(c) L-Abrine- Ile-Pro, 3- (3-thienyl)-L-alanine- Ile-Pro, 3- (2-furyl)-L-alanine- Ile-Pro, 2-Benzimidazoleacetic acid- Ile-Pro, 5-Hydroxytryptophan- Ile-Pro, Homotryptophan- Ile-Pro, Homophenylalanine- Ile-Pro, 1,2,3,4-tetrahydro isoquinoline-3-carboxylic acid- Ile-Pro, Azetidine-3-carboxylic acid- Ile-Pro, Cyclohexylalanine- Ile-Pro, 2-Oxo-4-phenyl-3-oxazolidine acetic acid- Ile-Pro, 4 – piperazine acetic acid- Ile-Pro.

(d) L-Abrine- Dap-Pro, 3- (3-thienyl)-L-alanine- Dap-Pro, 3- (2-furyl)-L-alanine- Dap-Pro, 2-Benzimidazoleacetic acid- Dap-Pro, 5-Hydroxytryptophan- Dap-Pro, Homotryptophan- Dap-Pro, Homophenylalanine- Dap-Pro, 1,2,3,4-tetrahydro isoquinoline-3-carboxylic acid- Dap-Pro, Azetidine-3-carboxylic acid- Dap-Pro, Cyclohexylalanine- Dap-Pro, 2-Oxo-4-phenyl-3-oxazolidine acetic acid- Dap-Pro, 4 – piperazine acetic acid- Dap-Pro.

(e) L-Abrine- Val-Trp, 3- (3-thienyl)-L-alanine- Val-Trp, 3- (2-furyl)-L-alanine- Val-Trp, 2-Benzimidazoleacetic acid- Val-Trp, 5-Hydroxytryptophan- Val-Trp, Homotryptophan- Val-Trp , Homophenylalanine- Val-Trp, 1,2,3,4-tetrahydro isoquinoline-3-carboxylic acid- Val-Trp, Azetidine-3-carboxylic acid- Val-Trp, Cyclohexylalanine- Val-Trp, 2-Oxo-4-phenyl-3-oxazolidine acetic acid- Val-Trp, 4 – piperazine acetic acid- Val-Trp.

(f) L-Abrine- Lys-Pro, 3- (3-thienyl)-L-alanine- Lys-Pro, 3- (2-furyl)-L-alanine- Lys-Pro, 2-Benzimidazoleacetic acid- Lys-Pro, 5-Hydroxytryptophan- Lys-Pro, Homotryptophan- Lys-Pro, Homophenylalanine- Lys-Pro, 1,2,3,4-tetrahydro isoquinoline-3-carboxylic acid- Lys-Pro, Azetidine-3-carboxylic acid- Lys-Pro, Cyclohexylalanine- Lys-Pro, 2-Oxo-4-phenyl-3-oxazolidine acetic acid- Lys-Pro, 4 – piperazine acetic acid- Lys-Pro.

(g) L-Abrine- Lys-Trp, 3- (3-thienyl)-L-alanine- Lys-Trp, 3- (2-furyl)-L-alanine- Lys-Trp, 2-Benzimidazoleacetic acid- Lys-Trp, 5-Hydroxytryptophan- Lys-Trp, Homotryptophan- Lys-Trp, Homophenylalanine- Lys-Trp, 1,2,3,4-tetrahydro isoquinoline-3-carboxylic acid- Lys-Trp, Azetidine-3-carboxylic acid- Lys-Trp, Cyclohexylalanine- Lys-Trp, 2-Oxo-4-phenyl-3-oxazolidine acetic acid- Lys-Trp, 4 – piperazine acetic acid- Lys-Trp.

(h) L-Abrine- Orn-Trp, 3- (3-thienyl)-L-alanine- Orn-Trp, 3- (2-furyl)-L-alanine- Orn-Trp, 2-Benzimidazoleacetic acid- Orn-Trp, 5-Hydroxytryptophan- Orn-Trp, Homotryptophan- Orn-Trp, Homophenylalanine- Orn-Trp, 1,2,3,4-tetrahydro isoquinoline-3-carboxylic acid- Orn-Trp, Azetidine-3-carboxylic acid- Orn-Trp, Cyclohexylalanine- Orn-Trp, 2-Oxo-4-phenyl-3-oxazolidine acetic acid- Orn-Trp, 4 – piperazine acetic acid- Orn-Trp.

(i) L-Abrine- Dap-Trp, 3- (3-thienyl)-L-alanine- Dap-Trp, 3- (2-furyl)-L-alanine- Dap-Trp, 2-Benzimidazoleacetic acid- Dap-Trp, 5-Hydroxytryptophan- Dap-Trp,

Homotryptophan- Dap-Trp, Homophenylalanine- Dap-Trp, 1,2,3,4-tetrahydro isoquinoline-3-carboxylic acid- Dap-Trp, Azetidine-3-carboxylic acid- Dap-Trp, Cyclohexylalanine- Dap-Trp, 2-Oxo-4-phenyl-3-oxazolidine acetic acid- Dap-Trp, 4 – piperazine acetic acid- Dap-Trp.

(j) L-Abrine- Ile-Phe, 3- (3-thienyl)-L-alanine- Ile-Phe, 3- (2-furyl)-L-alanine- Ile-Phe, 2-Benzimidazoleacetic acid- Ile-Phe, 5-Hydroxytryptophan- Ile-Phe, Homotryptophan- Ile-Phe, Homophenylalanine- Ile-Phe, 1,2,3,4-tetrahydro isoquinoline-3-carboxylic acid- Ile-Phe, Azetidine-3-carboxylic acid- Ile-Phe, Cyclohexylalanine- Ile-Phe, 2-Oxo-4-phenyl-3-oxazolidine acetic acid- Ile-Phe, 4 – piperazine acetic acid- Ile-Phe.

(k) L-Abrine-  $\beta$ -Ala-Pro, 3- (3-thienyl)-L-alanine-  $\beta$ -Ala-Pro, 3- (2-furyl)-L-alanine-  $\beta$ -Ala-Pro, 2-Benzimidazoleacetic acid-  $\beta$ -Ala-Pro, 5-Hydroxytryptophan-  $\beta$ -Ala-Pro, Homotryptophan-  $\beta$ -Ala-Pro, Homophenylalanine-  $\beta$ -Ala-Pro, 1,2,3,4-tetrahydro isoquinoline-3-carboxylic acid-  $\beta$ -Ala-Pro, Azetidine-3-carboxylic acid-  $\beta$ -Ala-Pro, Cyclohexylalanine-  $\beta$ -Ala-Pro, 2-Oxo-4-phenyl-3-oxazolidine acetic acid-  $\beta$ -Ala-Pro, 4 – piperazine acetic acid-  $\beta$ -Ala-Pro.

(l) L-Abrine- Pro-Pro, 3- (3-thienyl)-L-alanine- Pro-Pro, 3- (2-furyl)-L-alanine- Pro-Pro, 2-Benzimidazoleacetic acid- Pro-Pro, 5-Hydroxytryptophan- Pro-Pro, Homotryptophan- Pro-Pro, Homophenylalanine- Pro-Pro, 1,2,3,4-tetrahydro isoquinoline-3-carboxylic acid- Pro-Pro, Azetidine-3-carboxylic acid- Pro-Pro, Cyclohexylalanine- Pro-Pro, 2-Oxo-4-phenyl-3-oxazolidine acetic acid- Pro-Pro, 4 – piperazine acetic acid- Pro-Pro.

(j) L-Abrine- Cha-Trp, 3- (3-thienyl)-L-alanine- Cha-Trp, 3- (2-furyl)-L-alanine- Cha-Trp, 2-Benzimidazoleacetic acid- Cha-Trp, 5-Hydroxytryptophan- Cha-Trp,

Homotryptophan- Cha-Trp, Homophenylalanine- Cha-Trp, 1,2,3,4-tetrahydro isoquinoline-3-carboxylic acid- Cha-Trp, Azetidine-3-carboxylic acid- Cha-Trp, Cyclohexylalanine- Cha-Trp, 2-Oxo-4-phenyl-3-oxazolidine acetic acid- Cha-Trp, 4 – piperazine acetic acid- Cha-Trp.

Claim 6 (original) A peptidomimic compound according to claim 1 wherein the compound displays angiotensin converting enzyme (ACE) inhibiting activity.

Claim 7 (original) A peptidomimic compound according to claim 1 wherein the concentration of the peptidomimic compound for 50% inhibition of ACE activity ( $IC_{50}$ ) ranged from 2  $\mu$ mole to 10  $\mu$ mole in in-vitro condition using synthetic substrate Hippuryl-Histidyl-Leucine (HHL).

Claim 8 (original) A peptidomimic compound according to claim 1 wherein the dose of the synthesized ACE inhibiting peptidomimic compound which effectively blocked angiotensin converting enzyme ranges between 5- 8 mg/kg of body weight.

Claim 9 (currently amended/withdrawn) A process to synthesize the peptide derivative peptidomimics peptidomimic of claim 1, comprising

(a) coupling ACE inhibiting antihypertensive peptidomimic molecule wherein a heterocyclic or unusual amino acid present at ante-penultimate position is coupled to a dipeptide with amino acids present at ultimate position and penultimate position;

(b) synthesising dipeptide on a solid support by coupling and deprotection;

(c) coupling the heterocyclic or unusual amino acid to deprotected dipeptide at the N- $\alpha$  terminal of dipeptide;

(d) cleaving the synthesized peptidomimic compound of step (c) from solid support followed by purification and characterization;

Claims 10 - 17 (cancelled)

Claim 18 (currently amended) ~~Use of a~~ A method for inhibiting angiotensin converting enzyme in a mammal comprising providing the peptide derivative peptidomimic of claim 24, and administering the peptide derivative peptidomimic to the mammal having general formula ~~X-~~  $\text{CX}_1\text{-NH-AA}_1\text{-CONH-AA}_2$  ~~wherein X is a heterocyclic or unusual amino acid, X<sub>1</sub> is O or H<sub>2</sub> and AA<sub>1</sub> and AA<sub>2</sub> are amino acids as an angiotensin converting enzyme inhibitor.~~

Claim 19 (currently amended/withdrawn) ~~Use~~ The method according to claim 18 wherein the ~~dose of the synthesized ACE-inhibiting peptidomimic compound which effectively blocked the peptide derivative peptidomimic is administered to the mammal in a dose effective to block angiotensin converting enzyme ranges in the mammal, said dose ranging between 5- 8 mg/kg of body weight of the mammal.~~

Claim 20 (currently amended/withdrawn) Method for the inhibition of angiotensin converting enzyme in a subject suffering from hypertension comprising administering to the subject a pharmaceutically effective amount of the a peptide derivative peptidomimic of claim 1 having general formula ~~X-CX<sub>1</sub>-NH-AA<sub>1</sub>-CONH-AA<sub>2</sub> wherein X is a heterocyclic or unusual amino acid, X<sub>1</sub> is O or H<sub>2</sub> and AA<sub>1</sub> and AA<sub>2</sub> are amino acids to the subject with a pharmaceutically effective carrier.~~

Claim 21 (withdrawn) Method according to claim 20 wherein the subject is a mammal.

Claim 22 (withdrawn) Method according to claim 20 wherein the subject is a human being.

Claim 23 (currently amended/withdrawn) Method according to claim 20 wherein the peptide derivative peptidomimic is administered to the subject in a dose of the synthesized ACE inhibiting peptidomimic compound which effectively ~~blocked~~ blocks angiotensin converting enzyme in the subject, said dose ranging ranges between 5- 8 mg/kg of body weight of the subject.

Claim 24 (new). The peptide derivative peptidomimic according to claim 1, wherein AA<sub>1</sub> is ornithine and AA<sub>2</sub> is proline.

Claim 25 (new). The peptide derivative peptidomimic according to claim 24, wherein X is L-Abrine.

Claim 26 (new). The peptide derivative peptidomimic according to claim 1, which is represented by general formula X-CX<sub>1</sub>-NH-AA<sub>1</sub>-CONH-AA<sub>2</sub> wherein AA<sub>1</sub> is ornithine and AA<sub>2</sub> is proline.

Claim 27 (new). The peptide derivative peptidomimic according to claim 26, wherein X is L-Abrine.